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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/536,875

12/01/2006

Kristen Briggs

P0850.70005US01

6405

23628 7590 01/24/2011
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EXAMINER

WEN, SHARON X

ART UNIT

PAPER NUMBER

1644

MAIL DATE

DELIVERY MODE

01/24/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/536,875	Applicant(s) BRIGGS ET AL.	
	Examiner SHARON WEN	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 November 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 16, 17, 19-26, 28, 30, 31, 38-53, 67-69, 75 and 76 is/are pending in the application.
- 4a) Of the above claim(s) 10, 19-23, 30, 31, 47 and 67-69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11, 12, 16, 17, 24-26, 28, 38-46, 48-53, 75 and 76 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/7/2011</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment, filed 11/23/2010, has been entered.

Claims 13-15, 18, 27, 29, 32-37, 54-66, 70-74 and 77 have been canceled.

Claims 1-12, 16-17, 19-26, 28, 30-31, 38-53, 67-69, 75-76 are pending.

Applicant's election without traverse of Group I and species anti-herpes simplex virus antibody and glycan species 3Man, 2GlcNAc, 1Xyl in the replies filed on 02/19/2009, 05/29/2009 and 02/18/2010 is acknowledged.

Claims 10, 19-23, 30-31, 47, 67-69 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Inventions/species, there being no allowable generic or linking claim.

Claims 1-9, 11-12, 16-17, 24-26, 28, 38-46, 48-53 and 75-76 are currently under examination as they read on a plant-produced immunoglobulin.

This Action will be in response to Applicant's Arguments/Remarks, filed 11/23/2010.

The rejections of record can be found in the previous Office Action, mailed 05/25/2010.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 01/07/2011 has been considered by the examiner.

Claim Rejections - 35 USC § 112 second paragraph

The previous rejection under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment, filed 11/23/2010.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 11-12, 16, 24-26, 38-40, 42-43, 45-46, 48-53 and 75-76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated below for Applicant's convenience.

Although Applicant has elected species anti-herpes simplex virus antibody as the antigen-specific antibody, the present claims do not recite an antigen specificity for the claimed antibody. Therefore, the following grounds of rejection is set forth for an antibody without antigen-specificity.

Antibodies are glycoproteins that possess the ability to react in vitro and in vivo specifically and selectively with the antigenic determinants or epitopes eliciting their production or with an antigenic determinant closely related to the homologous antigen.

Antibodies are immunoglobulins that are formed in response to immunogens or that are screened for specificity an antigen / immunogen.

It has been well established in the art that the antigen binding specificity is critical to how the skilled artisan would employ antibodies in various modalities (e.g., affinity purification, detection or diagnostic assays, bioassays, treatment), including those consistent with the instant disclosure (see specification, including the Summary of the Invention).

However, the instant claims do not recite an antigen specificity for herpes simplex virus (HSV).

The specification provides insufficient direction or guidance regarding how to make and use antibodies in the absence of an antigen specificity for HSV and yet retain substantially the same binding specificity of the anti-HSV antibodies to used for treating HSV infection, which are enabling consistent with the disclosed utilities of the instant disclosure (see, e.g., paragraph [0252])

Given the well known polymorphism of antibodies, it would have been undue experimentation to make and use the vast repertoire of antibodies encompassed by the claimed invention in the absence of binding specificity for HSV to enable the scope of the claimed antibodies encompassed by the claimed invention.

Without sufficient guidance and given the well known complexity and unpredictability of using antibodies with no particular antigen specificity as well the well known polymorphism of antibodies; it would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly,

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extensive and undue to make and use the vast repertoire of antibodies broadly encompassed by the claimed invention in order to make and use the anti-HSV antibodies consistent with the instant disclosure.

With regards to the how-to-make prong of the enablement requirement, Applicant argues that one of skill in the art would readily know how to make any IgA immunoglobulin in plants in view of the description disclosed by the instant specification. With regards to the how-to-use prong of the enablement requirement, Applicant argues “that it is within the knowledge of a skilled artisan to use each individual IgA immunoglobulin within the scope of the rejected claims, based on the antigen-specificity of that individual IgA.”

In response to Applicant’s argument, it is noted that even Applicant acknowledges in the remarks that in order to use the antibody, one of skill would need to know the antigen-specificity of the individual immunoglobulin. Given that the present claims do not recite an antibody specificity, it would have been undue experimentation to use the vast repertoire of antibodies encompassed by the claims in the absence of binding specificity. Therefore, applicant’s argument has not been found convincing. The rejection is maintained.

Applicant is invited to amend the present claims by reciting the antigen-specificity, HSV, in order to obviate this rejection.

Claim Rejections - 35 USC § 102

The previous rejection under 35 USC 102(b) as being anticipated by Elbers et al. has been withdrawn in view of Applicant’s amendment, filed 11/23/2010

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9, 11-12, 16-17, 24-26, 28, 38-46, 48-53 and 75-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbers et al. (Plant Physiology, July 2001, 126:1314-1322, cited on IDS) in view of Mayfield et al. (US 2004/0014174).

Applicant's amendment necessitated the following new Grounds of Rejection.

Elbers et al. taught plant-produced immunoglobulins isolated from the plants that produced the immunoglobulin, wherein the immunoglobulins have at least one glycopeptide that lacks fucoses and wherein the glycan profile is the same or substantially the same as the structure in Figure 12 of the present application (see, e.g., page 1316, Composition of Complex N-Glycans; page 1317, Table 1, structure K; page 1320, Separation of IgG from Endogenous Glycoproteins of Tobacco Leaves). Given that the glycan profiled taught by Elbers are N-linked, the immunoglobulins comprising the N-linked glycan would have an asparagine (Asn) residue in CH2 region because by definition, N-linked means the glycan is attached to the nitrogen of the Asn residues in the Asn-X-Ser or Asn-X-Thr motifs. Moreover, given that N-linked glycans are also found in mammalian produced antibodies, the glycan with fucose found in Elbers's plant-produced immunoglobulin would be found attached to the same or substantially the same amino acid fragment such as the Asn-X-Ser or Asn-X-Thr motifs as the immunoglobulins produced in mammalian cells.

Furthermore, the plant-produced immunoglobulins taught by Elbers are IgG which would have a heavy and light chain as these are inherent properties of antibodies (see, e.g., page 1319, right column, third paragraph). Moreover, the glycan profile on Elbers's immunoglobulin was determined using MALDI-TOF analysis of free-N-linked glycans enzymatically-released from the antibody by trypsin digest (see page 1320 right column, Isolation of N-Linked Glycans).

Elbers et al. did not teach the antibody to be anti-herpes simplex virus antibody nor did Elbers et al. teach that the antibody is an IgA or a human antibody. However, it would have been obvious to one ordinary skill in the art to express an anti-HSV IgA antibody because Mayfield et al. taught expressing an anti-HSV monoclonal antibody in transgenic plants (see e.g., paragraph [0237]). Furthermore, Mayfield et al. taught

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engineering and an IgA antibody (paragraph [0018]) and human antibodies (paragraph [0084]). Moreover, Mayfield et al. taught expressing antibody fragments such as scFv that would have lack a tailpiece in plants.

Upon reading the teaching by Elbers and Mayfield, one of ordinary skill in the art would have been motivated to express an anti-HSV IgA human antibody in transgenic plants because plants are cost-efficient and contamination-safe factories for the production of recombinant proteins (see Elbers et al., page 1314, last paragraph). One of ordinary skill would also have reasonable expectation of success to produce the anti-HSV antibody in plants because many monoclonal antibodies have been successfully produced in plants such as that taught by Mayfield and also see Elbers et al. (page 1314, last paragraph). Given that glycan profiles are crucial for biological activity, stability, solubility, immunogenicity and plasma clearance of many glycoproteins, one of ordinary skill in the art would have been reasonably expected to engineer antibodies that have various glycan profiles such as that taught by Elbers (see Table 1) to optimize the antibody for its usages.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Argument

Applicant argues the following:

“First, the IgA antibody taught in Mayfield is a single-chain antibody expressed in plant chloroplasts. Paragraph [0018]. According to Mayfield, polypeptides expressed in plant chloroplasts “are not subject to certain post-translational modifications such as glycosylation.” Paragraph [0087]. Thus, unlike the claimed plant-produced IgA molecule or its heavy/light chain, the single-chain IgA antibody taught in Mayfield, expressed in chloroplasts, is non-glycosylated.

Second, Mayfield explicitly teaches that an advantage of the invention disclosed in it is to produce non-glycosylated polypeptides (e.g., a single-chain IgA antibody) in plants as such polypeptides can be expected to be less antigenic. Paragraph [0087]. This teaching indeed would have discouraged a skilled artisan from producing in glycosylated IgA immunoglobulins, as required by the claims under examination.”

In response to the first argument, it is first noted that the claims are broadly drawn to any plant-produced IgA comprising a glycopeptides profile with at least one glycopeptide that lacks fucose. Elbers taught the same or nearly the same glycopeptides profile except Elbers's antibody is an IgG not IgA. Elbers also taught that the glycoprotein profile of plant-produced immunoglobulins is important for pharmaceutical applications in terms of immunogenicity (see page 1315, left column, first paragraph). Mayfield taught generating anti-HSV IgA antibody with altered glycopeptide profile in order to reduce the immunogenicity of the antibody for therapeutic purposes. Both Elbers and Mayfield expressed desire to alter glycopeptides profile in plant-produced antibodies for therapeutic use with regards to immunogenicity. Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of both Elbers and Mayfield and produce an anti-HSV IgA antibody as taught by Mayfield with an altered glycopeptide profile as taught by Elbers.

The rationale to support a conclusion that the claims would have been obvious is that all the claimed elements (e.g., plant-produced immunoglobulin with altered glycopeptides profile / anti-HSV IgA produced in plant) were known in the prior art and one skilled in the art could have arrived at the claimed invention by using known methods as taught by Elbers and Mayfield with no change in their respective functions and the combination would have yielded nothing more than predictable results generating an anti-HSV IgA with altered glycopeptide profile.

The rationale to support a conclusion that the claims would have been obvious is that a method of decreasing the immunogenicity and providing a plant produced IgA antibody for therapy was made part of ordinary capabilities (e.g. recombinant plantibody technology) of one skilled in the art based upon the teachings of the prior art. One of ordinary skill in the art would have been capable of applying the known recombinant plantibody methods of producing antibodies with altered glycoprotein profile to decrease immunogenicity for therapy.

Given the strong motivation to combine the teaching to arrive the predictable conclusion as the antibody of the claimed invention, one of ordinary skill in the art would not bee been discouraged to apply the method taught by Elbers to make an antibody

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with altered glycopeptide profile to the anti-HSV antibody taught by Mayfield and the result would have been predictable to one of ordinary skill in the art.

Therefore, Applicant's argument has not been found convincing.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Primary Examiner, Art Unit 1644
January 21, 2011